



Attorney's Doc. No.: 00537-152001 / BPC017/

1634
#6

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Albert BEAUFOUR et al. Art Unit : 1634
Serial No. : 08/744,983 Examiner : J. Taylor
Filed : November 7, 1996
Title : METHOD OF IDENTIFYING PHARMACEUTICALS FROM PLANT
EXTRACTS

Commissioner for Patents
Washington, D.C. 20231

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RESPONSE

In response to the action mailed June 6, 2002 (the "Action"), please consider the following remarks:

REMARKS

Claims 1-6 are pending in the present application. All claims are rejected in the Office Action mailed June 6, 2002. For the reasons discussed below, Applicants respectfully request the rejections be withdrawn.

Rejection of claims 1-5 under 35 U.S.C. § 102(b)

Claims 1-5 are rejected under 35 U.S.C. § 102(b) as being anticipated by Chen et al. The Examiner asserts that Chen teaches all the limitations of 1-5. Applicants respectfully traverse the rejection.

It is stated in the Action that Chen et al. teach the limitations of claim 1 and dependent claims 2-5 where they teach "administering root extract of *S. lappa* Clarks to cells, and observing an anti-HBsAg effect (by measuring the amount of HBsAg in the cell, which is a protein, or the amount of RNA)." Applicants respectfully disagree. Chen does not teach the methods of claims

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1-5. Chen's methods measure the protein and mRNA levels of specific, predetermined molecules. Applicants' claim 1 recites isolating nonspecific protein(s) or RNA from extract-treated cells, further identifying the protein(s) or RNA that demonstrate different concentration levels in extract-treated, compared to nontreated, cells, and further identifying compound(s) within the extract that have the same effect.

In comparing a predetermined molecule, HBsAg or HBsAg mRNA, Chen fails to perform the step of "identifying which of said protein or RNA isolated from said plant extract treated cell type is not present in the same concentration in an untreated cell type." This is exemplified by the fact that the methods taught by Chen rely on prior knowledge of the molecules for which the concentration varies. For example, Chen uses enzyme immunoassays to determine HBsAg levels. In order to perform assays such as these, one must know the identity of the protein being examined as the assays rely on specific antibodies. This is distinguishable from Applicants' techniques, which do not analyze for a specific, predetermined molecule as Chen does. Applicants describe techniques that do not bias the identification of the molecules, such as 2-dimensional gel electrophoresis, Coomassie blue staining and silver staining. The specification does provide for generation of antibodies to isolated molecules to enable immunoaffinity purification for sequence analysis (see specification at pp.7-8). However, this is fundamentally distinct from the use of antibodies to determine protein concentration as taught by Chen.

Similarly, the assay used by Chen to compare HBsAg mRNA levels is dependent on prior knowledge of the molecule being examined. Chen uses Northern blot hybridization to measure quantities of HBsAg mRNA, which relies on the use of a specific HBV viral DNA probe. Applicants provide for methods such as subtractive hybridization, which do not rely on specific probes to compare mRNA quantities. Therefore, in failing to identify "which of said protein or RNA isolated from said plant extract treated cell type is not present in the same concentration..." as claimed, Chen does not teach all of the limitations of claims 1-5. Based on the foregoing, Applicants request that the Examiner withdraw this rejection.

Rejection of claim 6 under 35 U.S.C. § 103(a)

Claim 6 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Chen et al. in further view of Venkateswaran et al. The Examiner asserts that "Chen teaches measuring the suppression of HBsAg in cells using both a plant extract and a compound of the plant extract. It would have been obvious to measure the effect in vivo of the plant extract, as done by Venkateswaran, because it would have allowed one of ordinary skill in the art to measure the effects of a plant extract in vivo." Applicants respectfully traverse the rejection.

As discussed above, Chen does not teach the methods of claims 1-5. Chen teaches measuring the protein and mRNA levels of specific, predetermined molecules. Venkateswaran also describes the effects of plant extracts on specific, predetermined proteins. Thus, Chen and Venkateswaran together only teach analysis of predetermined molecules, and as such, do not suggest either alone or in combination the subject matter of Applicants' claim 6.

In addition, one would not be motivated to combine the teachings of Chen and Venkateswaran, as the nature of the compounds and assays used by Venkateswaran differ from those used by Chen. While Venkateswaran does administer plant extracts in vivo, Venkateswaran does not identify protein or RNAs that are "not present in the same concentration" as in untreated animals. Chen measures HBsAg protein and mRNA levels expressed in cells in response to plant extract treatment. Venkateswaran, on the other hand, does not measure expression levels of protein or mRNA in response to plant extract treatment. Venkateswaran measures the activity of a viral polymerase, DNAP. However, the reduced activity of DNAP is not necessarily related to a change in concentration of DNAP present, thus it provides no reliable measure of concentration.

Second, while both Chen and Venkateswaran examine the effect of plant extract compounds on viral surface antigen expression, both the nature of the compounds and the effect of these compounds on the viral surface antigens are completely different. For example, Venkateswaran examines the effect of *P. niruri* extract on WHsAg titer in woodchucks. Venkateswaran, et al. indicate that the reduction of WHsAg titer by *P. niruri* extract is not simply the result of altered expression of WHsAg. Instead, *P. niruri* extract directly interferes with binding between viral surface antigen proteins and antibodies reactive to these proteins

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(Venkateswaran, et al., Table 1). The reduced levels of WHsAg titers in extract-treated woodchucks may be due the reduction of DNAP activity in vivo and/or a complex combination of factors arising in vivo which result in reduced titers of woodchuck hepatitis virus. Thus, Venkateswaran is not looking at a measure that solely correlates with altered expression.

Chen does not teach the measurement of activity of viral polymerases, or the measurement of reduced viral titers in response to extract treatment. In fact, Chen points out that the compounds they have derived from a plant extract, "did not interfere with the enzyme immunoassay of HBsAg determination" (Chen et al, p. 102). Therefore, the compounds used by Chen do not affect HBsAg in the same manner as the compounds used by Venkateswaran.

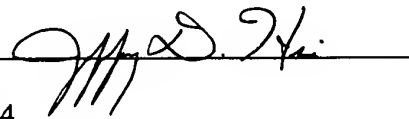
It is clear that Venkateswaran and Chen examine compounds with significantly different properties that require different methods to analyze. Thus, Applicants submit that the allegation in the Action that "it would have been obvious to measure the effect in vivo of the plant extract as done by Venkateswaran, because it would have allowed one of ordinary skill in the art to measure the effects of a plant extract in vivo" is inaccurate and unsupported in that it is not applicable to the claims and inappropriately combines the teachings of Chen and Venkateswaran. Therefore, Applicants request that the rejection of claim 6 be withdrawn.

Applicants ask that all claims be allowed. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing docket number 00537-152001.

Respectfully submitted,

Date: September 5, 2002

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